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EXAMINER	
MEHTA, ASHWIN D	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/24/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/914,001	KAEPPLER ET AL.
	Examiner	Art Unit
	Ashwin Mehta	1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 13-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1 and 5-12 in Paper No. 7 is acknowledged. Claims 2-4 and 13-21 are withdrawn from consideration as being drawn to non-elected inventions. Claims 5-12 should be amended so that it no longer depends from non-elected claim 3.

Priority

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). Applicants should insert a statement into the first line of page 1 of the specification, indicating that the instant application is a 371 of PCT/US00/2000, which claims the benefit of U.S Provisional Applications 60/ 169,858, filed 09 December 1999 and 60/123,888, filed 11 March 1999.

Specification

3. The specification fails to comply with the sequence rules of 37 CFR 1.821-1.825, because it presents sequences that are not referred to by their sequence identifiers (in the brief descriptions to Figures 1A-B, 2A-B, 3, 5, 8, 16, 17, 23, 24, and 25, on pages 15-21).

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, for example in Figure 6, line 13 of page 41, and line 29 of page 53. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

5. Claim 1 is objected to for failing to identify a nucleotide sequence by its sequence identifier, as required by 37 CFR

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1 and 5-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1: the recitation "stringent conditions" in line 3 renders the claim indefinite. It is not clear what conditions are defined as "stringent." The specification, in the paragraph spanning pages 11-12, indicates that generally stringent conditions are selected to about 5°C to about 20°C lower than the thermal melting point at a defined ionic strength and pH. However, the ionic strength and pH are not defined. Typical conditions are provided. However, other conditions that would be considered as "stringent" are not defined. It is suggested that the

following recitation be inserted after "stringent conditions": --that comprise at least one wash under conditions comprising 0.2X SSC at 65°C.

In claim 5: the claim states that it is drawn to a recombinant expression cassette comprising the isolated and purified nucleic acid sequence of claim 1. However, claim 1 is directed to an isolated and purified DNA sequence. The DNA sequence of claim 1 hybridizes to the nucleic acid sequence of Figure 1A. It is then not clear if the recitation "isolated and purified nucleic acid sequence" in lines 1-2 of claim 5 is referring to the DNA sequence in line 1 of claim 1, or the nucleic acid sequence in Figure 1 A mentioned in line 2 of claim 1. For examining purposes, claim 5 will be examined as if the recitation "nucleic acid sequence" in lines 1-2, 3, and 3-4 actually read --DNA sequence--.

In claim 11: The claim is a "Markush" type claim that used incorrect Markush terminology. The term "and" in line 4 should be replaced with --or--.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1 and 5-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any isolated and purified DNA sequence which encodes a Zea mays zmet2a methyltransferase and which hybridizes to the nucleic acid shown in Figure 1A under any stringent condition; or a recombinant expression cassette comprising said isolated and purified nucleic acid sequence operably linked to any promoter sequence and any polyadenylation sequence; and a bacterial cell, transgenic plant, and seed comprising said recombinant expression cassette.

The specification indicates that a Zea mays cDNA was isolated which codes for a methyltransferase termed Zmet2a. The coding region of the cDNA is shown in Figures 1A and 1B (page 36, line 25 to page 37, line 11). The corresponding genomic clone was also isolated (page 37, lines 13-27). The Zmet2a gene has 20 exons, 19 introns, and the inferred protein, using the first predicted ATG, is composed of 912 amino acids (page 40, line 31 to page 41, line 7). The gene also has a second, downstream, predicted start site that codes for an enzyme of 809 amino acids (page 41, lines 10-19). Zmet2a mutant plants, in which a Mutator insertion is found within one of the exons, have reduced methylation of CpNpG sites in the genome (page 42, line 1 to page 45, line 12). The specification indicates that the Zmet2a protein has 10 domains: domains I and X bind to AdoMet, the source of the methyl group for transfer; domain IV has a catalytic domain; domain VI aids in positioning of domain IV; domain VIII aids in binding by neutralizing the negative charge of the DNA phosphodiester backbone; the region between domains VIII and IX defines sequence specificity; chromodomains lie within amino acids 366-379 and 380-388 (page 25, lines 3-26).

However, the specification does not describe other isolated and purified DNA sequences encoding other Zmet2a methyltransferases. The specification does not describe other DNA

sequences that encode a protein that has the same activity as that encoded by the sequence shown in Figure 1A. Further, the claims do not define the stringency conditions, and therefore encompass any hybridization condition. It is well established in the art that moderate stringency hybridization conditions will allow the binding of unrelated sequences. See Fiers vs. Sugarno, 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Given the breadth of the claims encompassing any isolated DNA sequences hybridizing with the sequence shown in Figure 1A under any stringent condition, and the lack of written description as discussed above, the specification fails to provide an adequate written description of the multitude of nucleic acids encompassed by the claims.

8. Claims 1 and 5-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid sequence shown in Figure 1A, does not reasonably provide enablement for other isolated DNA sequence hybridizing with the nucleic acid sequence in Figure 1A, or transgenic plants or seeds comprising the nucleic acid sequence shown in Figure 1A or DNA sequences that hybridize to it. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn towards any isolated and purified DNA sequence which encodes a Zea mays zmet2a methyltransferase and which hybridizes to the nucleic acid shown in Figure 1A under any stringent condition; or a recombinant expression cassette comprising said

isolated and purified nucleic acid sequence operably linked to any promoter sequence and any polyadenylation sequence; and a bacterial cell, transgenic plant, and seed comprising said recombinant expression cassette.

As discussed above, the specification teaches that a Zea mays cDNA was isolated which codes for a DNA methyltransferase termed Zmet2a. The coding region of the cDNA is shown in Figures 1A and 1B (page 36, line 25 to page 37, line 11). The corresponding genomic clone was also isolated (page 37, lines 13-27). The Zmet2a gene has 20 exons, 19 introns, and the inferred protein, using the first predicted ATG, is composed of 912 amino acids (page 40, line 31 to page 41, line 7). The gene also has a second, downstream, predicted start site that codes for an enzyme of 809 amino acids (page 41, lines 10-19). Zmet2a mutant plants, in which a Mutator insertion is found within one of the exons, have reduced methylation of CpNpG sites in the genome (page 42, line 1 to page 45, line 12).

However, the specification does not teach other isolated and purified DNA sequences encoding Zea mays Zmet2a methyltransferases. The claims encompass DNA sequences that will hybridize to that in Figure 1A under any stringency condition. However, it is well established in the art that low to moderate stringency conditions will allow the binding of sequences that are unrelated to the template sequence. It is suggested that claim 1 be amended as mentioned above. Further, the specification does not teach other Zmet2a methyltransferases. See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).It is suggested that claim 1 be amended as mentioned above.

The specification also teaches that transgenic plants expressing the claimed DNA sequences in a tissue-specific manner can be used to silence a target gene in that tissue, due to an increase in methylation (paragraph bridging pages 35-36). However, the specification does not actually demonstrate that expression of any target gene was silenced in any transgenic plants. The specification does not teach that any transgenic plants were made at all. It is not clear that transgenic expression of the claimed DNA sequences can be used to control expression of a target gene in the manner contemplated by the specification. Martienssen et al. (Curr. Opin. Genet. Devel., 1995, Vol. 5, pages 234-242) for example, teach that copy number, rather than extensive DNA methylation, appears to be the critical factor in the silencing of transgenes, and that many examples of transgene silencing do not involve DNA methylation (page 236, 2nd column, last paragraph and page 237, 1st column, 1st paragraph). Further, non-target genes would also be affected in the claimed transgenic plants and seeds. Finnegan et al. (Annu. Rev. Plant Physiol. Plant Mol. Biol., 1998, Vol. 49, pages 223-247) discuss how DNA methylation may affect plant development (pages 233-236, for example). The specification does not teach what the affect of overexpression of the claimed DNA sequences would be on the plant itself. As DNA methylases have a role in transcriptional regulation, it is not clear what the affect of overexpressing the claimed DNA sequences would be on the development of the plant or parts thereof, or even if the plant would be viable. In the absence of further guidance, it would require undue experimentation by one skilled in the art to produce the claimed transgenic plants in which only the intended target gene is silenced. The specification does not teach other ways in which the claimed transgenic plants and seeds should be used. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the

knowledge of one skilled in the art" must supply the enabling aspects of the invention. Given the breadth of the claims encompassing any isolated DNA sequences hybridizing with the sequence shown in Figure 1A under any stringent condition and transgenic plants or seeds comprising a recombinant expression cassette comprising the claimed DNA sequences, unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

9. The claims are deemed free of the prior art. The prior art teaches an isolated DNA sequence encoding an Arabidopsis DNA methyltransferase (Finnegan et al. 1996, Proc. Natl. Acad. Sci., USA, Vol. 93, pages 8449-8454). However, the prior art does not teach or fairly suggest isolated nucleic acid sequences encoding a Zea mays zmet2a methyltransferase, or the nucleic acid sequence shown in Figure 1A.

10. Claims 1 and 5-12 are rejected. Claims 2-4 and 13-21 are withdrawn for being drawn to non-elected inventions.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M.. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this

application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

September 16, 2002

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER